Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks herein, is respectfully requested. Claims 66-67, 70-74, and 88 are amended, and claims 1-65, 68-69, 75-87 and 89 are canceled; as a result, claims 66-67, 70-74 and 88 are now pending in this application. The amendments are intended to advance the application and are not intended to concede to the correctness of the Examiner's position or to prejudice the prosecution of the claims prior to amendment, which claims are present in a continuation of the above-identified application.

The amendments to claims 70-74 and the cancellation of claim 69 obviate the objection to claims 69-74 under 37 C.F.R. § 1.75(c) noted at page 5 of the Office Action.

The amendments to claim 66 are supported, e.g., at page 9, lines 29-32 and page 25, lines 27-30 of the specification.

The amendments to claims 70-74 are supported, e.g., at page 51, line 29 of the specification.

Amended claim 88 is supported by Figure 18B of the specification.

The specification is amended to address the Examiner's objections indicated in items 5-8 of the Office Action.

Substitute Figure 22T and substitute Figure 22B are enclosed herewith.

The 35 U.S.C. § 101 Rejection

The Examiner rejected claims 66-74 and 86-88 under 35 U.S.C. § 101 because the claimed invention is allegedly not supported by either a specific, asserted utility or a well established utility. This rejection is respectfully traversed.

The Utility Examination Guidelines of the U.S. Patent and Trademark Office explicitly state that "the reasonable assignment of a new protein to [a] class of sufficiently conserved proteins [on the basis of sequence homology] would impute the same specific, substantial, and credible utility to the assigned protein." Utility Examination Guidelines, *Fed. Reg.* 66:1092-1099, at 1096, column 3 (2001). The specification discloses that the nucleic acid molecules of the invention encode polypeptides that catalyze the synthesis of polyketides such as the ones with a bryopyran ring (page 2, lines 17-19). Figure 13 discloses that contig 5B (which includes

SEQ ID NO:37) corresponds to sequences in the 3' two-thirds of the bryostatin gene cluster and encodes sequences related to polyketide synthases (PKS) based on sequence homology (page 5, lines 24-25). The utility for such nucleic acids is well-established, e.g., to recombinantly produce the product of the PKS (see, e.g., Kao et al., Science, 265:509 (1994), a copy of which is enclosed herewith).

As the specification provides a specific, asserted utility for the claimed subject matter, withdrawal of the § 101 rejection is respectfully requested.

The 35 U.S.C. § 102(b) Rejection

The Examiner rejected claims 66-69 and 86-87 under 35 U.S.C. § 102(b) as being anticipated by GenBank Accession No. U65015 (*Vibrio furnissii* GlcNAc-6-P-deacetylase (manD), 1996) as evidenced by Kerr et al. (Tetrahedron Letters, 37:8305 (1996)). This rejection is respectfully traversed.

GenBank Accession No. U65015 teaches a DNA sequence encoding a *Vibrio furnisii* N-acetylglucosamine 6-phosphate deacetylase which is associated with a N-acetyl glucosamine utilization pathway. Although Kerr et al. disclose that acetate may be a precursor employed in bryostatin 1 synthesis (page 8307), neither GenBank Accession No. U65015 nor Kerr et al. disclose an isolated nucleic acid molecule that encodes at least one polypeptide that catalyzes at least one step in the synthesis of at least one bryopyran ring.

Accordingly, withdrawal of the rejection under 35 U.S.C. § 102(b) is respectfully requested.

The 35 U.S.C. § 112, Second Paragraph, Rejections

The Examiner rejected claims 66-74 and 86-87 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. This rejection, as it may be maintained with respect to the pending claims, is respectfully traversed.

The cancellation of claims 68-69 and 86-87 render the § 112(2) rejection as it relates to those claims moot.

The amendment to claim 66, to delete the phrases "derived from" and "marine organism", obviate the § 112(2) rejections relating to those phrases.

The Examiner alleges that the phrase "at least one polypeptide that catalyzes at least one step in the synthesis of at least one polyketide or bryopyran ring" is unclear as to its metes and bounds and that no polyketide synthase polypeptides are described as being encoded by SEQ ID NO:37.

It is Applicant's position that the metes and bounds of the claims in view of the specification are clear. Figure 2 shows the domain structure encoded by three open reading frames for a bryopyran synthase, including the enzyme activities of each domain, which catalyze the initial steps in bryostatin synthesis. SEQ ID NO:37 (described in Figure 18B) is included in clone 5B (page 60, lines 17-18), which corresponds to the 3' two-thirds of the bryostatin gene cluster, and by visual inspection has three open reading frames. Figure 13 shows the location of clone 5B in the bryostatin gene cluster and regions in the cluster which have homology to PKS. Thus, one of ordinary skill in the art in possession of Applicant's specification would be apprized of the metes and bounds of the phrase "at least one polypeptide that catalyzes at least one step in the synthesis of at least one bryopyran ring" and the polypeptides encoded by SEQ ID NO:37.

In view of the amendments and remarks herein, withdrawal of the rejections under 35 U.S.C. § 112, second paragraph, is respectfully requested.

The 35 U.S.C. § 112, First Paragraph, Rejections

The Examiner rejected claims 66-74 and 86-88 under 35 U.S.C. § 112, first paragraph, alleging that since the claimed invention is not supported by either a specific, asserted utility or a well established utility, one skilled in the art would not know how to use the claimed invention. This rejection is respectfully traversed.

As discussed above, the claimed invention is supported by a specific, asserted utility. Moreover, the use of polyketide synthase genes is well know to the art (see, e.g., U.S. Patent Nos. 5,849,541, 6,022,731, and 6,033,883, a copy of each is enclosed herein). Thus, the claimed invention is fully enabled by the present specification.

The Examiner also rejected claims 66-74 and 86-87 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

The cancellation of claims 68-69 and 86-87 renders the § 112(1) "written description" rejection of those claims moot.

The Examiner asserts that claim 66 is drawn to a polynucleotide claimed solely by function with no structural limitations. As amended, claim 66 is directed to a composition comprising at least one isolated nucleic acid that encodes at least one polypeptide that catalyzes at least one step in the synthesis of at least one bryopyran ring, or the complement thereof, wherein the at least one polypeptide comprises at least one activity of a polyketide synthase, wherein the at least one nucleic acid molecule hybridizes under hybridization conditions of 0.015 M NaCl/0.0015 M sodium citrate, 0.1% SDS at 50°C to SEQ ID NO:37 or the complement thereof. Thus, Applicant has described at least one species of the genus and identified the common characteristics of the claimed molecules, i.e., they encode at least one polypeptide that catalyzes at least one step in the synthesis of at least one bryopyran ring, and hybridize to SEQ ID NO:37 or the complement thereof.

Accordingly, withdrawal of the § 112(1) rejections is respectfully requested.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-373-6959) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

MARGO HAYGOOD ET AL.,

By their Representatives,

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Date August 5, 2003

By _____
Janet E. Embretson
Reg. No. 39,665

CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner of Patents, Washington, D.C. 20231, on this 5th day of August, 2003.

Candis B. Buending
Name

_____
Signature

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Lys Leu Gly Asp Pro Ile Glu Val Glu Thr Leu Ala Glu Ser Phe Arg
 1               5                  10                  15

Val Tyr Thr Asp Lys Arg His Tyr Cys Ala Leu Gly Ser Val Lys Ser
            20                  25                  30

Asn Ile Gly His Leu Gly Val Gly Ala Gly Ile Ala Gly Val Thr Lys
        35                  40                  45

Val Leu Leu Ser Leu Gln His Arg Met Leu Pro Pro Thr Ile His Cys
    50                  55                  60

Glu Asp Val Asn Pro Gln Ile Ala Leu Glu Gly Ser Pro Phe Tyr Ile
65                  70                  75                  80

Asn Thr Glu Leu Lys Pro Trp Gln Ser Gly Asp Gly Ile Pro Arg Arg
                85                  90                  95

Ala Gly Val Ser Ser Phe Gly Val Ser
        100                 105
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SEQ ID NO: 110

FIG. 22T

SEQID NO:24 26

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Pro Leu Gly Asp Pro Ile Glu Met Ala Ala Leu Lys Gln Ala Phe Gly
 1               5                  10                  15

Thr Gln Lys Lys Lys Tyr Cys Ala Ile Gly Ser Val Lys Ser Asn Ile
            20                  25                  30

Gly His Ala Asp Thr Ala Ala Gly Val Ala Gly Leu Ile Lys Thr Val
        35                  40                  45

Met Ala Leu Lys Ala Arg Gln Ile Pro Pro Ser Leu His Phe Glu Thr
    50                  55                  60

Pro Asn Pro Gln Ile Asp Phe Ala Asp Ser Pro Phe Tyr Val Asn Thr
65                  70                  75                  80

Thr Leu Lys Asp Trp Asn Thr Asn Gly Val Pro Arg Arg Ala Gly Val
                85                  90                  95

Ser Ser Phe Gly Ile Gly
            100
```

FIG. 22BB